Call for technical data on the permitted food additives potassium nitrite (E 249), sodium nitrite (E 250), sodium nitrate (E 251) and potassium nitrate (E 252)

Published: 7 December 2022

Deadline: 18 January 2023

Background

According to Article 32 of Regulation (EC) No 1333/2008[1], food additives permitted in the EU before 20 January 2009 should be subject to a new risk assessment by the European Food Safety Authority (EFSA). The programme for the re-evaluation of these permitted food additives has been set up by Commission Regulation (EU) No 257/2010[2].

In most cases, EFSA confirms the safety of the food additives at their currently reported uses and use levels. However, for some additives EFSA has identified issues that require a follow-up. Additional specific data is needed to address those issues.

The additives whose safety re-evaluation by EFSA was hindered by limited data availability, but which are not expected to pose an immediate food safety concern, are not going to be immediately removed from the Union list of permitted additives, or their uses and/or use levels revised. Instead, business operators are requested to indicate to the Commission their interest in the continuity of approval of the additive(s) under re-evaluation and in providing, by a certain deadline, the data needed by EFSA to complete its risk assessment. In general, new toxicological studies will be needed to generate these missing data.

Once EFSA has assessed the new data, the current authorisation of the additive(s) may be revised, if needed.

If business operators do not provide the requested data (by the predefined deadline) the present authorisation will be revised based on EFSA's current scientific opinion and the additive(s) may be removed from the Union list of permitted additives. The same applies if the new data submitted is not sufficient for EFSA to conclude the risk assessment, since there will be no successive requests for additional data.

Food additives for which EFSA has identified concerns in terms of exposure or specifications will be subject to the same follow-up approach, but EFSA's assessment of the new data may not always be needed.

The Commission will undertake that the time assigned for addressing issues identified by EFSA is as short as possible and dependent on the time needed to generate and assess the required new data.

EFSA's Scientific Opinion on the re-evaluation of potassium nitrite (E 249) and sodium nitrite (E 250) as food additives and its Scientific Opinion on the re-evaluation of sodium nitrate (E 251) and potassium nitrate (E 252) as food additives

EFSA's Panel on Food Additives and Nutrient Sources added to Food (ANS) delivered a Scientific Opinion re-evaluating the safety of potassium nitrite (E 249) and sodium nitrite (E 250) when used as a food additive in June 2017[3].

[1] OJ L 354, 31.12.2008, p. 16.
[2] OJ L 80, 26.3.2010, p. 19.
[3] EFSA Journal 2017;15(6):4786 (https://www.efsa.europa.eu/en/efsajournal/pub/4786)

The Panel concluded that an increased methaemoglobin level, observed in human and animals, was a relevant effect for the derivation of the acceptable daily intake (ADI). The Panel, using a benchmark dose modelling approach, derived an ADI of 0.07 mg nitrite ion/kg bw per day. The exposure to nitrite resulting from its use as food additive did not exceed this ADI for the general population, except for a slight exceedance in children at the highest percentile. However, if all sources of dietary nitrite exposure were considered the ADI would be exceeded for infants, toddlers and children at the mean and for all age groups at the highest exposure. The Panel assessed the endogenous formation of nitrosamines from nitrites based on the theoretical calculation of the N-nitrosodimethylamine (NDMA) produced upon ingestion of nitrites at the ADI and estimated a margin of exposure (MoE) > 10,000. The Panel estimated the MoE to exogenous nitrosamines in meat products to be < 10,000 in all age groups at high level exposure. Based on the results of a systematic review, it was not possible to clearly discern nitrosamines produced from the nitrite added at the authorised levels, from those found in the food matrix without addition of external nitrite. In epidemiological studies there was some evidence to link (i) dietary nitrite and gastric cancers and (ii) the combination of nitrite plus nitrate from processed meat and colorectal cancers. There was evidence to link preformed NDMA and colorectal cancers.

EFSA recommended that the European Commission considers lowering the current limits for toxic elements (lead, mercury and arsenic) in the EU specifications for nitrites (E 249–E 250) in order to ensure that nitrites (E 249–E 250) as a food additive will not be a significant source of exposure to those toxic elements in food.

In the same period, EFSA's ANS Panel delivered a Scientific Opinion re-evaluating the safety of sodium nitrate (E 251) and potassium nitrate (E 252) when used as a food additive[4].

The current ADIs for nitrate of 3.7 mg/kg body weight (bw) per day were established by the SCF (1997) and JECFA (2002). The available data did not indicate genotoxic potential for sodium and potassium nitrate. The carcinogenicity studies in mice and rats were negative. The Panel considered the derivation of an ADI for nitrate based on the formation of methaemoglobin, following the conversion of nitrate, excreted in the saliva, to nitrite. However, there were large variations in the data on the nitrate-to-nitrite conversion in the saliva in humans. Therefore, the Panel considered that it was not possible to derive a single value of the ADI from the available data. The Panel noticed that even using the highest nitrate-to-nitrite conversion factor the methaemoglobin levels produced due to nitrite obtained from this conversion would not be clinically significant and would result to a theoretically estimated endogenous N-nitroso compounds (ENOC) production at levels which would be of low concern. Hence, and despite the uncertainty associated with the ADI established by the SCF, the Panel concluded that currently there was insufficient evidence to withdraw this ADI. The exposure to nitrate solely from its use as a food additive was estimated to be less than 5% of the overall exposure to nitrate in food based on a refined estimated exposure scenario. This exposure did not exceed the current ADI (SCF, 1997). However, if all sources of exposure to dietary nitrate are considered (food additive, natural presence and contamination), the ADI would be exceeded for all age groups at the mean and the highest exposure.

EFSA recommended that the European Commission considers lowering the current limits for toxic elements (lead, mercury and arsenic) in the EU specifications for nitrates (E 251–E 252) in order to ensure that nitrates (E 251–E 252) as a food additive will not be a significant source of exposure to those toxic elements in food.

Overall purpose of this call for data

To give the opportunity to business operators to submit the technical data needed to address issues identified by EFSA in the re-evaluation of the safety of nitrites and nitrates (E 249-252) as food additives.

[4] EFSA Journal 2017;15(6):4787 (https://www.efsa.europa.eu/en/efsajournal/pub/4787)

Information required for the food additives potassium nitrite (E 249), sodium nitrite (E 250), sodium nitrate (E 251) and potassium nitrate (E 252)

With reference to the conclusions and recommendations in the Scientific Opinion on the re-evaluation of potassium nitrite (E 249) and sodium nitrite (E 250) as a food additive and in the Scientific Opinion on the re-evaluation of sodium nitrate (E 251) and potassium nitrate (E 252) as a food additive, information for these food additives is sought on:

1. Technical data for the revision of the specifications for potassium nitrite (E 249), sodium nitrite (E 250), sodium nitrate (E 251) and potassium nitrate (E 252)

   The characterisation of all the different commercial preparations of the food additives potassium nitrite (E 249), sodium nitrite (E 250), sodium nitrate (E 251) and potassium nitrate (E 252) from non-consecutive batches of each preparation, in relation to:

   - Analytical data, if possible supported by certificate of analysis, on current levels of arsenic, lead and mercury in commercial samples of the food additives;
   - The lowest technologically achievable level for arsenic, lead and mercury in order to adequately propose maximum limits in the specifications.

The analyses should be performed with appropriate analytical methods applying state of the art techniques. Specific data on the methods of analysis used should be provided. These include, but are not limited to, e.g. the principle of the method, the scope of the method (i.e. the range of sample types that the method is used for), the concentration units used to express the analytical result(s), validation of the method (in particular limit of detection (LOD) and (LOQ).

Procedure of the call for data

It should be noted that this call concerns only technical data. Therefore, the 2-step procedure used in previous calls for scientific and technical data is not followed, since such procedure is considered to be more appropriate for calls for data requesting scientific data (e.g. toxicological data which require that new toxicological studies are performed). Therefore, the deadline of this call is the final deadline for submission of the requested technical data.

Business operators are requested to submit to the Commission by **18 January 2022** the above-requested data.

In order to streamline the data collection exercise, business operators are invited to liaise with the relevant food business operator associations for the data submission. In particular, data providers shall ensure that the same data are not sent several times to the European Commission (for example, they should not be sent by both the business operator and also by the association to which the business operator belongs to).

Any questions about this call for data should be sent to the email address Sante-E2-Additives@ec.europa.eu.

Submission of the required data

Business operators are requested to submit the above-indicated data by the agreed deadline using the online platform CIRCABC. The "Guidance for online data submission on Food Improvement Agents via CIRCABC Sante-Cad-In Group"[5] provides practical information on how to use the CIRCABC platform for the online submissions.

[5] https://ec.europa.eu/food/sites/food/files/safety/docs/fs_food-improvement-agents_guidance_circabc_data-sub.pdf

Common electronic formats (e.g. MS Office®, Adobe Acrobat Reader®) allowing content copying and printing (no content copy protection) should be used for the files to be submitted. The text of the files should be searchable using the search facilities of standard software packages. The submission should include a cover letter stating clearly in the subject line the food additive(s) to which it refers, and describing the data submitted. The cover letter should provide the contact details of the data submitter and should be addressed to:

Bruno Gautrais, Head of Unit E2
European Commission
Directorate-General for Health and Food Safety
Directorate E – Food and feed safety, Innovation
Unit E2 – Food Processing Technologies and Novel Foods
B-1049 Brussels

This cover letter should also be sent separately to the functional mailbox SANTE-E2-Additives@ec.europa.eu.

Once the new data are received, they will be submitted to EFSA for evaluation and preparation of a scientific opinion, if appropriate.

Confidential data

According to article 8 of Regulation (EU) No 257/2010 setting up a re-evaluation programme of approved food additives, interested business operator or other interested party may submit a request to treat certain parts of the information or data submitted in accordance with this Regulation as confidential. Such requests shall be accompanied by verifiable justifications. The confidentiality requests shall be assessed in accordance with Article 12 of Regulation (EC) No 1331/2008, which shall apply *mutatis mutandis*.

Possibility for EFSA to use the data for the safety assessment of the same substance under other legal or regulatory frameworks

In line with Union policy objectives on animal welfare and testing on vertebrates, EFSA aims to avoid the duplication of testing on vertebrates, and to achieve an optimal use of the relevant financial and human resources by the private sector. Therefore, in anticipation of cases where EFSA may be interested in using or reusing relevant information or data (i.e. technical, toxicological data) for the evaluation of the same substance under a different legal or regulatory framework from the one mentioned above, or for the evaluation of another substance under the same or different legal framework as above, please indicate explicitly in writing, whether by participating in the voluntary submission of relevant data or information, you also give EFSA the permission to use and/or reuse these data for other EFSA safety assessments, and/or for a data sharing exercise with third parties or other international bodies.